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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,181	09/15/2003	Steven Z. Wu	50623.334	1431

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
10/14/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/663,181	WU ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,30-32 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,30-32 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response after Non-Final Office Action filed 06/16/09 is acknowledged.

Claims 25, 30-32 and 34 are pending in this application. No amendments to the claims have been made herein. Claims 1-24, 26-29 and 33 were previously cancelled. Claims 25, 30-32 and 34 remain rejected.

* * * * *

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 25, 30-32 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter *et al.* (hereinafter "Hunter") (U.S. Pat. No. 5,886,026).

Hunter ('026) teaches methods for treating angiogenic-dependent diseases and compositions comprising anti-angiogenic factors and polymeric carriers, stents which have been coated with such compositions and methods for utilizing these stents and compositions (see column 1, lines 15-20); (col.3, line 42 - col. 5, line 43). Methods for the preparation of drug-loaded microspheres, films and pastes are also disclosed (see Examples).

The anti-angiogenic compositions may be fashioned in the form of microspheres of any size ranging from 50 nm to 500 μm (col. 17, lines 31-44). The compositions may also be prepared in paste or gel forms or as films (col. 17, line 45 - col. 18, line 10); (col. 37, lines 33-45). The anti-angiogenic compositions may be administered in combination with

pharmaceutically or physiologically acceptable carriers, excipients or diluents (col. 37, lines 46-59).

Suitable polymeric carriers taught include poly(D,L-lactic acid), poly(glycolic acid), polycaprolactone, gelatin, starch, cellulose and polysaccharides for example and blends thereof (col. 16, lines 36-61). The anti-angiogenic compositions comprise a variety of active compounds in addition to the anti-angiogenic factors and polymeric carriers. Suitable active compounds are disclosed at column 15, lines 16-40).

The stents may be coated with the anti-angiogenic compositions or anti-angiogenic factors in a variety of ways, such as: (a) by directly affixing to the stent an anti-angiogenic composition (e.g., by either spraying the stent with a polymer/drug film or by dipping the stent into a polymer/drug solution), (b) by coating the stent with a substance such as a hydrogel which will absorb the anti-angiogenic composition or anti-angiogenic factor; (c) by interweaving the anti-angiogenic composition coated thread (or the polymer itself formed into a thread) into the stent structure, (d) by inserting the stent into a sleeve or mesh which is comprised of or coated with an anti-angiogenic composition or (e) constructing the stent itself with an anti-angiogenic composition (col. 22, lines 45-66).

The Examples at columns 42 onwards demonstrate various methods for the preparation of the anti-angiogenic compositions. For instance, Example 3 at column 42 demonstrates methods for the encapsulation of suramin whereby a polymer mixture is combined with the active agent (suramin) and solvent or reagent - dichloromethane (DCM). The process yields microspheres, wherein the polymer (PVA) encapsulates the active agent – suramin. Similarly, Example 4 at columns 42-43 demonstrates a procedure for the encapsulation of paclitaxel.

Example 8 at columns 45-47 outlines the manufacture of microspheres. Example 9 at columns 47-48 presents a process for the manufacture of a stent coating, wherein a sufficient quantity of polymer and DCM are added in a vial and mixed by hand in order to dissolve the polymer. An appropriate amount of paclitaxel is added to the solution and dissolved by hand shaking. The stent is coated using a horizontal spraying technique, whereby the polymer and drug are deposited on the stent.

Procedures for producing a film are discussed at columns 51-52. The films may be made by for example, casting and spraying. In the casting technique, polymer is either melted and poured into a shape or dissolved in DCM and poured into a shape. The polymer then either solidifies as it cools or solidifies as the solvent evaporates. In the spraying technique, the polymer is dissolved in solvent and sprayed onto glass, as the solvent evaporates the polymer solidifies on the glass. Repeated spraying enables a buildup of polymer into a film that can be peeled from the glass (col. 51, lines 55-63).

Also see Example 14 at columns 60-61, which demonstrates thermopastes made up of polymer (PCL containing MePEG) loaded with paclitaxel.

Procedures for producing a nanopaste are discussed at columns 52-53. The nanopaste is a suspension of microspheres suspended in a hydrophilic gel. The gel or paste can be smeared over tissue as a method of located drug-loaded microspheres close to the target tissue.

Example 11 at columns 53-57 demonstrate controlled delivery of paclitaxel from microspheres composed of a blend of biodegradable poly(D,L-lactic acid) (PLA) polymer and non-degradable ethylene-vinyl acetate (EVA) copolymer. The microspheres are prepared by a solvent evaporation method.

The instant invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made given the teachings of Hunter. Hunter teaches methods for the preparation of drug-loaded microspheres, which are provided as a coating onto a stent, whereby the drug (i.e., paclitaxel) is dissolved in a polymer solution containing a polymer and solvent (DCM), and wherein the solvent is evaporated to yield microspheres. Hunter teaches that the compositions can be in suitable forms, such as, for example, a paste, as in the form of a suspension wherein the microspheres are suspended in a hydrophilic gel, and thereafter the gel or paste can be smeared over tissue. Hunter also discloses compositions in the form of a film, whereby polymer is dissolved in a solvent, the solvent then evaporates and the polymer solidifies to form a film that can subsequently be peeled. The methods of Hunter are useful and effective for the treatment of angiogenic-dependent diseases and thus would include restenosis, as is instantly claimed.

* * * * *

Response to Arguments

Applicant's arguments filed 16 June 2009 have been fully considered but they are not persuasive.

- **Rejection under 35 U.S.C. 103(a) over Hunter (US 5,886,026).**

Applicant argued, "The Examiner has not established a *prima facie* case of obviousness with respect to claim 25 because all of the elements have not been addressed and the cited prior art does not teach or suggest those elements. In the sections cited by the Examiner, the prior art teaches dissolving a therapeutic substance in a carrier polymer and coating the resulting solution on the stent, rather than creating a suspension of the therapeutic substance and a

polymer, and coating the suspended therapeutic substance on the stent. This is contrary to the method in claim 25, wherein the polymeric particles containing the therapeutic substance are suspended in the polymeric material dissolved in the solvent."

Applicant's arguments have been fully considered but they are not persuasive. It is noted that Hunter teaches dissolution of the therapeutic substance in a carrier polymer as in Example 9 and subsequently coating the solution onto the stent. However, the argument that a suspension of the therapeutic substance and polymer is not taught by Hunter was not deemed persuasive because the reference also recognizes and teaches methods for preparing various compositions such as nanopastes which are comprised of a suspension of microspheres that are suspended in a hydrophilic gel. See for instance, columns 52-53. The gel or paste can then be smeared over tissue as a method of locating drug-loaded microspheres close to the target tissue. Thus, the reference is well aware of employing a suspension of microspheres with a polymeric gel and hence, would read on a "suspension" as sought by Applicant. The pastes disclosed by Hunter would be comprised of a suspension whereby particles of active agent would be suspended. See col. 17, line 45 - col. 18, line 10; col. 37, lines 33-45. Furthermore, the prior art's method of preparation yields an end result essentially the same as that desired in the instant invention. Namely, the end result being a layer containing particles of polymer combined with the therapeutic substance. As a result, there would be no functional difference between the methods disclosed by Hunter and that of the present invention; the end product being a coating layer of drug and polymer.

For these reasons, the rejection of record has been maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

- No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday-Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Humera N. Sheikh/

Primary Examiner, Art Unit 1615

hns

October 09, 2009